Acta Oncologica 29 (1990) Fasc. 7

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CARCINOMA OF THE HYPOPHARYNX

A retrospective analysis of the treatment results over a 25-year period

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Abstract

One hundred and sixty-two patients treated for hypopharyngeal cancer during the 25-year period 1958–1982 were reviewed retrospectively. Of the 162 patients, 29 received combined treatment with surgery and postoperative irradiation, 106 received radical radiotherapy alone, and 27 palliative radiotherapy. The 5-year survival rate was 28% for the patients treated with combined therapy and 16% for the patients treated with radical radiotherapy. There were no long-term survivors in the palliatively treated group. The major cause of death was tumour (102 patients) while 40 patients died of intercurrent diseases.

Key words: Hypopharyngeal cancer, surgery, radiation therapy, treatment results.

Cancer of the hypopharynx is a dangerous tumour which often presents with locally advanced stage. Many patients have multiple medical problems associated with tobacco and alcohol abuse. Hypopharynx is generally divided into three anatomic regions (1): the pharyngo-oesophageal junction (postcricoid area), the piriform sinus, and the posterior pharyngeal wall. Sometimes it is not possible to state the site of origin of the primary tumour since it is too extensive.

The present study is a retrospective analysis of treatment results in patients with carcinoma of the hypopharynx seen in our department during the period 1958–1982.

Material and Methods

Patients. During the period 1958–1982, 181 new patients with histologically verified squamous cell carcinoma of the hypopharynx were treated at the Department of Radiotherapy and Oncology, Helsinki University Central Hospital, Helsinki, Finland. The 19 patients who had distant metastasis at the time of presentation, had previous malignancies other than skin cancer, or had another simultaneous cancer were excluded from the present study. Thus, 162 patients were evaluated. There were 102 males (63%) and 60 females (37%) with a mean age of 63 years (SD ± 12 years, range 31–83). During the same years, totally 192 new patients with hypopharyngeal cancer were reported to the Finnish Cancer Registry from the same geographical area (unpublished data, 1989). The distribution of the tumours by primary site and sex of the patients was as follows: postcriciod area 48 (30%), of which 20 in males and 28 in females; piriform sinus 84 (52%), of which 66 in males and 18 in females; and posterior pharyngeal wall 30 (18%), of which 16 in males and 14 in females. The distribution of patients according to the TNM classification (UICC, 1982) is presented in Table 1. The TNM-classification of malignant tumours from 1982 (1) was used since the regional nodes were not regularly measured. Totally 77 patients (48%) presented at the admission to therapy with cervical adenopathy. Only three patients with postcorticoid cancer were reported to have had Plummer–Vinson syndrome.

Treatment. The treatment varied with stage of the primary lesion and presence, size, and mobility of cervical metastatic lesions, the patient's overall health and, at times, the patient's preference. Of the 162 patients, 29 (18%) received combined treatment with surgery and postoperative radiotherapy, 106 (65%) received radical radiotherapy only, and 27 (17%) radiotherapy with purely palliative intent (Table 2).

In the 29 patients (19 males and 10 females) with surgery and postoperative radiotherapy the tumours had

Accepted for publication 13 November 1989.

Table 1

The distribution of 162 patients with carcinoma of the hypopharynx according to the TNM classification (UICC, 1982)

	TNM classification				
	T1	T2	T3	T4	Total
N0	8	28	29	20	85
N1	2	22	12	4	40
N2	0	8	1	8	17
N3	0	6	4	10	20
Total	10	64	46	42	162

Table 2

Distribution of 162 hypopharyngeal tumours by stage (UICC, 1982) and treatment

	Stage				
Treatment	I	II	III	IV	Total
Surgery with postoperative radiotherapy	2	4	15	8	29
Radical radiotherapy alone	6	24	41	35	106
Palliative radiotherapy	0	0	9	18	27
Total	8	28	65	61	162

the following primary sites: five in the postcricoid area, 22 in the piriform sinus and two in the posterior pharyngeal wall. All tumours were radically operated with total laryngectomy and partial or total pharyngectomy as the preferred surgical modality. If nodes were positive for disease, a radical neck dissection was usually performed. Totally 23 neck dissections were performed, which in 22 patients were unilateral and in one patient bilateral. The postoperative irradiation was started within two months after surgery. The median target dose through parallel opposed portals to upper neck at the midplane with ^{60}Co was 56.6 Gy (range 36.0–68.2) within 5.4 weeks (range 3.7–7.1) given in 5 fractions per week, the median fraction size was 2.1 Gy (range 1.5–2.8). The maximum dose (d_{max}) in the lower neck was 51 Gy in 17 fractions given through one anterior field.

In the 106 patients (67 males and 39 females) with radical radiotherapy only, 35 tumours were situated in the postcricoid area, 45 in the piriform sinus and 26 in the posterior pharyngeal wall. Of the patients in this group, 95 were treated with ^{60}Co, 8 with 20 MV photons from a betatron and 3 with 6 MV photons from a linear accelarator. All patients were irradiated from two parallel opposed lateral portals with field size depending on disease extent. Usually the target volume included the primary tumour and at least the upper and middle cervical nodes. The dose was calculated at the midplane. The mean height of the treatment field was 10.5 cm (SD $\pm$ 2.4) and the mean field size was 80.4 cm^2 (SD $\pm$ 5.1).

In the 85 patients with clinically negative nodes, N0, the lower neck was irradiated through one anterior field to the maximum dose (d_{max}) of 51 Gy in 17 fractions. The 57 patients which had N1–2 disease received 60–65 Gy as target dose. The treatment of N3 disease (20 patients) was individualized, based on the extension of the lymph node metastases.

Continuous treatment was given to 45 (42%) patients with a median tumour dose of 58.4 Gy (range 45.8–70.6) and a median daily dose of 2.1 Gy (range 1.7–2.5) given in 5 fractions per week over 5.6 weeks (range 4.8–7.1). A randomized clinical trial was performed from 1964 to 1967 to compare split-course with continuous radiotherapy. The results of this study have been published previously (2), and the efficacy of these two treatment modalities is not compared in the present analysis. Split-course therapy was used from 1967 as the routine treatment and only four patients were treated with continuous therapy after 1967. To compensate for the rest period, the total dose was increased by 5–10% as recommended by Holsti (3). The planned tumour dose in the split-course therapy was 66 Gy with a daily fraction of 2.2 Gy given in 5 fractions per week in 8–9 weeks with 2–3 weeks' rest in the middle of the treatment.

Split-course therapy was given to 61 (58%) patients with a median tumour dose of 64.2 Gy (range 49.2–73) and a median daily dose of 2.2 Gy (range 1.9–2.5) given in 5 fractions per week in 8.4 weeks (range 5.1–9.6) with 2.7 weeks' (range 2.2–3.2) rest in the middle of the treatment.

In 49 patients (46%) the primary tumour received a total dose ranging from 55 to 65 Gy, in 35 patients (33%) this dose ranged from 45 to 54 Gy, and in 22 patients (21%) from 66 to 73 Gy.

Palliative radiotherapy was given to 27 patients (16 males and 11 females) of which 8 had primary tumours in the postcricoid area, 17 in the piriform sinus and two in the posterior pharyngeal wall. The median tumour dose in the upper neck was 32.4 Gy (range 8.2–44.2) within 3.6 weeks (range 1.1–4.2) given in 5 fractions per week.

Follow-up of the patients. All patients were regularly seen at 3-monthly intervals during the first 3 years after the treatment and then at 6-monthly intervals. After 5 years the controls were performed at regional health centres with reporting to our department.

Statistics. Actuarial survival was determined without correction for age or intercurrent death from the date of initiation of therapy (the date of the primary operation in the combined therapy group or the date of initiation of radiotherapy in the radiotherapy groups) until the date of the last follow-up examination or death respectively. All the patients had a 5-year minimum follow-up (mean 11.9). The survival rates were computed by using the product-limit estimator of Kaplan & Meier (4). The statistical difference between survival curves was calculated with and Mantel–Cox's test, the χ^2-test was used to compare

response rates, and Student's t-test for comparing doses (5). Data were analysed using a BMDP (Biomedical Computer Programs-P series) statistical package.

Results

Survival. The 5-year survival rate was 28% for the patients treated with surgery plus postoperative irradiation and 16% for the patients treated with radical radiotherapy. There were no long-term survivors in the palliative group ($p < 0.001$. Fig. 1). The 5-year survival rate was 11% for the total patient material and 18% for the patients treated with curative intent. There was no obvious difference in survival between male and female patients, totally and in the various subgroups. The expected 5-year survival for the normal population of the same sex and age composition from the same years was 86%.

The 5-year survival rate was 32% for stage I, 24% for stage II, 16% for stage III and 8% for stage IV in patients treated with radical radiotherapy alone ($p < 0.05$, Fig. 2) and the 5-year survival rates by sites of the primary tumours were 18% for the postcricoid area, 10% for the piriform sinus and 14% for the posterior pharyngeal wall ($p = 0.511$, Fig. 3).

Postoperative radiotherapy. In the 29 patients having combined treatment, the median total dose of postoperative radiotherapy for the tumours (n = 13) with local control was 59.2 Gy (range 50.3–68.2), whereas it was 47.7 Gy (range 36.0–66) for the tumours (n = 16) developing local failure ($p < 0.01$). The lower doses were due to acute mucosal reactions and/or decline of patients' general condition.

Complications. In 16 (15%) out of 106 patients treated with radical radiotherapy it was not possible to complete the planned course of radiation treatment due to acute mucosal reaction (n = 1) and poor general condition (n = 5). In addition, 17 (16%) patients had unplanned interruption in the radiation treatment because of mucositis; after a pause, these patients completed radiotherapy up to the planned dose. In the group with combined treatment 4 patients had late complications, but there were no surgical deaths. The late complications included two fistulas, one stricture and one carotid artery blowout. In the 106 patients treated with radical radiotherapy alone more pronounced mucosal atrophy or oedema was observed in 11 patients (10%), soft tissue necrosis occurred in two patients. There was no case of late nervous tissue damage.

Recurrence and death. After initial therapy, excluding the patients treated palliatively, 75 patients (56%) received secondary treatment for recurrent or residual disease. Of these patients, 67 (89%) had evidence of recurrence within 24 months, and 70 (93%) within 36 months. The recurrences were as a rule irradiated with doses about 30 to 40 Gy; eight patients were also operated. No secondary lymph node dissections were performed. All 75 patients died from their disease.

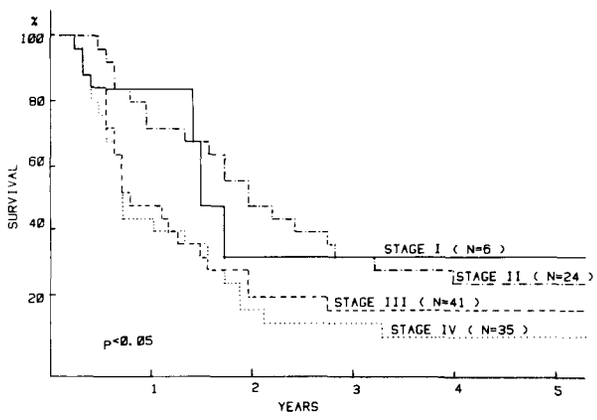

Fig. 2. Survival curves by stage for 106 patients with carcinoma of the hypopharynx treated with radical radiotherapy alone.

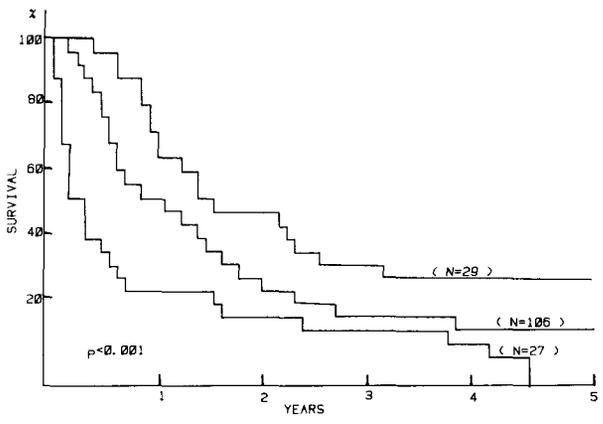

Fig. 1. Survival curves for 162 patients with carcinoma of the hypopharynx by different treatment modalities. Surgery + postoperative irradiation (n = 29), radical radiotherapy (n = 106), palliative radiotherapy (n = 27).

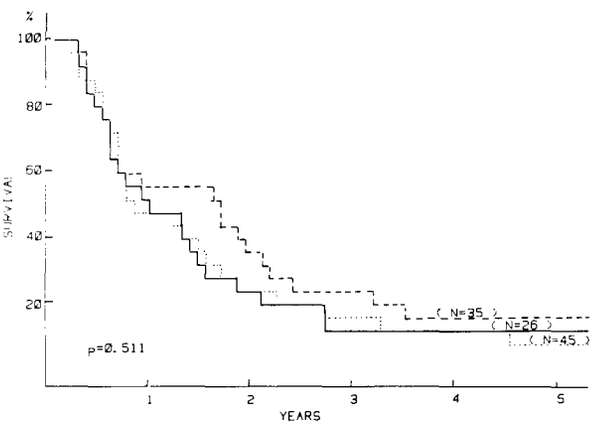

Fig. 3. Survival curves by primary site for patients with carcinoma of the hypopharynx treated with radical radiotherapy alone. Postcricoid area (n = 35), piriform sinus (n = 45) and posterior pharyngeal wall (n = 26).

During the 5-year follow-up, 142 of the 162 patients treated died from various causes. Sixty-one patients died from uncontrolled primary lesion, 24 from uncontrolled primary lesion and neck node metastases, 4 died from uncontrolled neck node metastases and 13 patients from distant metastases. Thirty-seven patients died from intercurrent disease and three patients committed suicide. In the present study, 11 (7%) out of 162 patients developed a second primary malignant neoplasm in the upper aerodigestive tract during follow-up.

Discussion

There is no agreement as to the best treatment for hypopharyngeal cancer. Patient selection for treatment modalities, treatment timing, and dosage of radiation vary among institutions and oncologists. Very often, discrepancies between results in different series reflect more the selection of patients than the efficacy of different treatment modalities. Most studies, including the present one, are retrospective and not randomized.

Only three patients in the present series were reported to have Plummer–Vinson syndrome. They had noted difficulties in swallowing for several years. Plummer–Vinson syndrome is rare in Finland as pointed out by Mustakallio already in 1944 (6). Tobacco and alcohol abuse was common in the present series but has not been further analysed.

A review of the literature on the treatment of the carcinoma of the hypopharynx reveals widely differing 5-year survival rates. The results presented for radiation therapy in particular show wide variation. Jacobsson (7), using a cross-fire 180 kV technique with 4 fields, reported a 14% 5-year disease-free survival. Kirchner (8) reported a 4% 3-year disease-free survival rate while Ahmad & Fayos (9) reported 40% actuarial 5-year survival rate in 199 patients. The present analysis describes the results obtained in a large cancer centre serving nowadays a population of approximately 1.5 million people. As a result of an agreed policy between all centres within the geographical area, almost all patients registered with the diagnosis of squamous cell carcinoma of the hypopharynx were treated with radiation therapy. Therefore, our results probably reflect rather closely the results in an unselected group of patients.

The 5-year survival rate for the 106 patients treated with radical radiotherapy (Fig. 1) was 16%. This figure is close to that reported by Keane et al. (10) which included all patients seen within a defined geographical area.

The survival rates for different anatomic regions (Fig. 3) were rather similar in the group of patients treated with radical radiotherapy alone. This is in agreement with some results published in the literature (11, 12) whereas Ahmad & Fayos (9) reported that tumours of the upper hypopharynx had significantly better survival than tumours of the lower hypopharynx.

Preoperative radiation has not been used at our department, because of difficulty in scheduling patients for immediate surgery and institutional interest in the use of postoperative radiation. In the group of patients with combined therapy, the median total dose of postoperative radiotherapy for the tumours with local control was significantly higher (59.2 Gy) than for those with local failure (47.7 Gy). This is in agreement with McComb & Fletcher (13), who concluded that the dose of postoperative radiotherapy should be 60 Gy in 6 weeks, whereas Arriagada & Eschewege (14) felt that doses of more than 45 Gy may be beneficial.

According to Wang (15) the daily dose should not exceed 1.8 Gy per fraction when 5 treatments per week are given. Million & Cassisi (16) found that the acute side effects were quite tolerable with 1.8–1.9 Gy/fraction. The fraction size commonly used in the present series was 2.1–2.2 Gy. Wang (15) recommended 65 Gy in 7 weeks for treatment with curative intent. The median total dose in the present series varied from 58.4 to 64.2 Gy given in from 5.6 to 8.4 weeks. The influence of overall treatment time on local control and survival was not analysed in this material since this has been done and reported recently in a larger material of head and neck cancer (2). There is some clinical evidence, that protracting the overall treatment time can increase the probability of local failure (17). However, there is also some evidence that a 10% increase in total dose may compensate for the tumour cell proliferation during a 2–3 weeks' split-course interval (2). It has been stated, at least for squamous carcinomas of head and neck, that the delivery of a described fractionated dose regimen should be given without unnecessary interruptions and in the shortest possible time that is tolerated by late-responding normal tissues (18).

The treatment results in hypopharyngeal cancer are still very poor and further improvement of the therapeutic methods is needed. Hyperfractionated radiotherapy has been tried and improved local control has been reported from some studies (19, 20). Chemotherapy regimens with efficiency in squamous cell carcinoma (as cisplatin + 5-FU (21, 22)) have been developed but their value in hypopharyngeal cancer in combination with surgery and/or radiotherapy is still to be settled.

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